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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/598,482

02/06/2007

Philip Wilson Howard

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EXAMINER

KIFLE, BRUCK

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

11/24/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/598,482	Applicant(s) HOWARD ET AL.	
	Examiner Bruck Kifle	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 August 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 13-21, 23, 25-29, 31 and 32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 13-21, 23, 25-29, 31 and 32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>08/18/08</u> . | 6) <input type="checkbox"/> Other: _____ |

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Applicant's amendments and remarks filed 08/26/08 have been received and reviewed.

Claims 1-8, 13-21, 23, 25-29, 31 and 32 are now pending in this application.

Claim Rejections - 35 USC § 112

Claims 1-8, 13-21, 23, 25-29, 31 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

i) In claim 1 the phrase "or pharmaceutically acceptable salts or solvates" should be rewritten as, for example, "or a pharmaceutically acceptable salt thereof" to comply with proper Markush language. See below rejections regarding "solvates."

iii) The "optionally substituents" listed in the independent claims are not all radicals. Some are classes of compounds with no point of attachment to the rest of the molecule and others are ions or have dangling valencies. See, for example, ether, acetal, hemiacetal, imidic acid, ester, sulfate, disulfide, etc. Appropriate listing of the desired substituents is required.

vi) Claims 26 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are still the reaction steps (the removal step of R₁₄ in claim 26 and the replacement of Y-R"-Y' to X'-R"-X in claim 29).

Claims 1-8, 13-21, 23, 25-29, 31 and 32 are again rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutically acceptable salt, does not reasonably provide enablement for solvates of the compound of formula Ia and Ib. The specification does not enable any person skilled in the art to which it pertains, or with which

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it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicants have not shown how one skilled in the art can arrive at a given solvate. The basis of this rejection is the same as given in the previous office action and is incorporated herein fully by reference.

Applicant's arguments have been fully considered but not found persuasive. The claims, insofar as they embrace solvates are not enabled. The numerous examples presented all failed to produce a solvate. The evidence of the specification is thus clear: These compounds do not possess the property of forming solvates; there is no evidence that such compounds even exist. Thus, this is a circumstance where the "specification is evidence of its own inadequacy" (*In re Rainer*, 377 F.2d 1006, 1012, 153 USPQ 802, 807). These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance appears to be true here: there is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

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Claims 8, 9, 13-16 and 18-21 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Smellie et al. (Biochemistry (2003), 42(27), 8232-8239). The reference teaches the compound of formula 2d (see page 8232). The claims differ by requiring a C₈ linker between the PBD moieties over the prior art C₆ linker. It has been long established that structural relationship varying the size of a linking carbon chain - is per se obvious.

Applicants argue that it is unpredictable and unobvious whether or not such changes in a PBD dimer would affect the ability of the compound to bind DNA and also argue superior results. This must be shown, in a comparative, side-by-side testing and not merely asserted.

Therefore, in the absence of a showing that the linker with 8 carbons of the instant application demonstrate unexpected and unobvious results over the linker with 6 carbons of the reference, the claims are deemed obvious thereover. Applicants must prove that their compounds possess a property that the prior art compounds do not possess, not is not disclosed to possess. In re Dillon (16 USPQ 1897) states "the discovery that a claimed composition possesses a property not disclosed for the prior art subject matter does not by itself defeat a prima facie case."

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle whose telephone number is 571-272-0668. The examiner can normally be reached on Mondays-Fridays from 8:30 AM -6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bruck Kifle/
Primary Examiner
Art Unit 1624

BK
November 19, 2008